REMARKS

Claims 1, 3-7, and 9-17 are pending in this application. Claims 1, 3-4, and 9-12 have been amended and claims 2 and 8 have been canceled without acquiescence and without prejudice. Claims 18-38 have been canceled without prejudice and without acquiescence, as they are drawn to a non-elected invention. Applicants retain the right to file divisional and/or continuation applications on any canceled subject matter. No new matter has been added.

The outstanding issues are as follows:

- The Specification is objected under 37 CFR 1.821(d) for failing to disclose SEQ ID NOS for the nucleic acid sequences disclosed on pages 41 and 42.

- Claims 1-17 have been rejected under 35 USC 112, first paragraph for allegedly containing subject matter which was not described in such a way as to enable one skilled in the art.

- Claims 1-17 have been rejected under 35 USC 112, first paragraph for allegedly containing subject matter which was not described in such a way as to reasonable convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention.

- Claims 1-17 have been rejected under 35 USC 102(e) as allegedly being anticipated by US Patent 6,420,526 or US Patent 6,504,010.

Applicants respectfully traverse the outstanding rejections, and Applicants respectfully request reconsideration and withdrawal thereof in light of the remarks contained herein.

I. Specification Objection

The Examiner has objected to the specification under 37 CFR 1.821 (d) for failing to disclose SEQ ID NOS for the nucleic acid sequences disclosed on pages 41 and 42. Applicants are confused by this objection. A sequence listing was filed with the application containing all the sequences. Yet further, upon review of pages 41 and 42, it appears that all sequences are identified by SEQ ID NOS. Applicants request that the Examiner identify the specific sequences by paragraph number.

II. 35 U.S.C. §112, first paragraph

A. Enablement

Claims 1-17 are rejected under 35 USC 112, first paragraph as containing subject matter which was not described in such a way as to enable one of skill in the art to make and/or use the invention. The Examiner indicates that the specification disclosure does not enable one skilled in the art to practice the invention without an undue amount of experimentation. Applicants respectfully traverse.

Applicants remind the Examiner that an invention need not be reduced to practice prior to filing (*Gould v. Quigg*, 822 F.2d 1074, 1078, 3 USPQ 2d 1302, 1304 (Fed. Cir. 1987)). Yet further, the specification need not contain an example if the invention is otherwise disclosed in such manner that one skilled in the art will be able to practice it without an undue amount of experimentation. *In re Borkowski*, 422 F.2d 904, 908, 164 USPQ 642, 645 (CCPA 1970).

Applicants refer the Examiner to the enclosed Declaration by Marie-Claude Gingras and to Bouchon et al., Nature 410:1103-1107, 2001. Applicants assert that Bouchon et al utilized the teachings of the present invention to show that a soluble TREM-1 receptor inhibits cell functions that are activated by TREM-1 (for example, reduced the activity of TREM-1/DAP12 complex, and reduced inflammation). Thus, the soluble TREM-1 receptor of Bouchon et al. was acting as a competitive inhibitor, as described by the present application.

Applicants assert that the quantity of experimentation needed to be performed by one skilled in the art is only one factor involved in determining whether undue

experimentation is required to make and use the invention. An extended period of experimentation may not necessarily be undue if sufficient direction or guidance is provided. Applicants assert that the methods outlined in the specification provide skilled artisans sufficient directions to enable the modulation of the immune response by administering a compound that decreases the activity of DAP12/TREM-1 complex, as illustrated by Bouchon et al. *In re Colianni*, 561 F.2d 220, 224, 195 U.S.P.Q. 150, 153 (CCPA 1977). Thus, the amount of experimentation is permissible because it is merely routine and the specification provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. *In re Wands*, 858 5F.2d 731, 737, 8 U.S.P.Q.2D 1400, 1404 in (Fed. Cir. 1988). In light of the data presented by Bouchon et al., Applicants assert that the present invention is enabled since one of skill in the art was able to practice the invention without undue experimentation.

Yet further, Applicants are confused by the statements made by the Examiner on page 4 of the Office action. It appears that the Examiner is requiring human trials as the only sufficient support for what the Examiner perceives is enablement of the claims. This is an absolutely improper standard. Although it is expected that pharmaceutical inventions will necessitate further research and development, clinical testing is not required to obtain a patent. *In re Brana*, 51 F.3d 1560, 1569 (Fed. Cir. 1995). Applicants are not required to perform FDA-type testing on humans in order to obtain a patent. The Examiner in this instance appears to be confusing the requirements under the law for obtaining a patent with the requirements for obtaining government approval for marketing drugs. *Id. at 1568.*

> We hold as we do because it is our firm conviction that one who has taught the public that a compound exhibits some desirable pharmaceutical property in a standard experimental animal has made a significant and useful contribution to the art, even though it may eventually appear that the compound is without value in the treatment in humans.

Id. at 1667, citing In re Krimmel, 292 F.2d 948, 952 (CCPA 1961).

In light of the above arguments, Applicants assert that the claims are enabled and respectfully request that the rejection be withdrawn.

B. Written Description

Claims 1-17 are rejected under 35 USC 112, first paragraph as containing subject matter which was not described in such a way as to convey to one of skill in the art that the inventors had possession of the claimed invention.

Applicants assert that the description of the function of the compound provides sufficient written description. *See In re Smythe, 480 F.2d 1376, 1383, 178 USPQ 279, 285 (CCPA 1973).* Techniques in molecular biology and protein chemistry are, and were at the time of the application, well known and understood in the art. Applicants assert that one of skill in the art would be able to follow the guidelines established in the specification to produce compounds that would result in the desired function. For example, the Specification in paragraphs [0069]-[0081] provides guidelines that are used to produce biological function equivalents of SEQ. ID. NO. 2.

In view of the above arguments, Applicants respectfully request that the rejection be withdrawn.

III. 35 U.S.C. § 102

Claims 1-17 are rejected under 35 U.S.C. § 102(e) as being anticipated by US patent 6,420,526 or US Patent 6,504,010. Applicants respectfully traverse.

Applicants did not receive the attached sequence alignment mentioned by the Examiner. SEQ. ID. NO. 2 of the present application is 150 amino acids in length compared to 234 amino acids in length of SEQ. ID. NO. 478 and 1825. Applicants request that these alignments be forwarded to the undersigned. In the meantime, Applicants note that from amino acid 137 to amino acid 150, the is very little similarity between SEQ. ID. NO. 2 and SEQ. ID. NO. 478 or 182.

Applicants remind the Examiner that in order to anticipate a claim, the reference must teach each and every element as set forth in the claim. *Verdegaal Bros. V. Union Oil Col. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

In order to advance prosecution of the present application, claims 1-11 have been amended without prejudice and without acquiescence. Independent claims 1 and 7 are drawn

to administering a compound that is a competitive inhibitor of the ligand to TREM-1 to decrease the activity of DAP12/TREM-1 thereby resulting in a decrease in myeloid cell activation and/or an inflammatory resposne. Applicants assert that at best '526 teaches a sequence similar to TREM-1 or SEQ. ID. NO. 1 that may be involved in the activation of neutrophils, however, it does not teach nor does it make inherent that competitively inhibiting the ligand for TREM-1 or SEQ. ID. NO. 1 would result in a decrease in myeloid cell activation. Applicants assert that '526 teaches that the polynucleotides and polypeptides are useful as reagents for diagnostic procedures (See column 139, lines 21-25); useful in the expansion of stem cells and progenitors cells (See column 140 lines 1-2); and useful in the differentiation and/or proliferation of various cell types (See column 140, lines 3). The other item mentioned in '526 is that the proteins, as well as, antibodies directed against the proteins may be useful as tumor markers and/or immunotherapy targets. No where in the application can the Applicants find a teaching that a competitive inhibitor for SEQ. ID. NO. 478 is used nor a teaching that would make an inhibitor of the ligand to TREM-1 inherent.

Regarding '010, Applicants assert that '010 teaches the use of the polynucleotide and/or polypeptide compositions as immunogenic compositions (column 45, lines 13-15, column 78, lines 61-65; and column 79, lines 15-17). An immunogenic composition is a composition that produces immunity or evokes an immune response (See Dorland's Medical Dictionary, page 880). Still further, '010 states in column 45, lines 30-35

> An "immunogenic portion", as used herein, is a fragment of an immunogenic polypeptide of the invention that itself is immunologically reactive (i.e., specifically binds) with the B-cells and/or T-cell surface antigen receptors that recognize the polypeptide.

Applicants assert that the purpose of '010 is not similar to the claims of the present invention. Although SEQ. ID. NO. 1825 may be similar to TREM-1 or SEQ. ID. NO. 1, the claims of the present invention are drawn to decreasing an immune response or myeloid cell activation by administering an inhibitor to the TREM-1 ligand resulting in a decrease in the activity of DAP12/TREM-1 complex. This is the opposite of '010 which teaches generation of an immune response using polypeptides, such as SEQ. ID. NO. 1825. Thus, '010 does not teach nor inherently teach the present invention.

If the Examiner continues to maintain a rejection that relies on inherency, Applicants respectfully request the Examiner to point to the page and line of '526 and/or '010 that justifies the rejection. See *Ex parte Schricker*, 56 USPQ2d 1723 (B.P.A.I. 2000).

In view of the above arguments, Applicants respectfully request that the rejection be withdrawn.

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to pass this application to issue.

Applicant believes no fee is due with this response. However, if a fee is due, please charge our Deposit Account No. 06-2375, under Order No. 10023489 from which the undersigned is authorized to draw.

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Respectfully submitted,

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combined i., deficiency of lymphoid cells that mediate both antibody (B-lymphocytes) and cellular (T-lymphocytes) immunity. See table. Called also *combined immunodeficiency disease.*

common variable i. (CVID), common variable unclassifiable i., a heterogeneous group of disorders characterized by hypogammaglobulinemia, decreased antibody production in response to antigenic challenge, and recurrent pyogenic infections, and often associated with hematologic and autoimmune disorders. Most patients have normal numbers of circulating B cells, which can identify antigens and proliferate, but lack plasma cells and appear to have an intrinsic defect of B cell differentiation. However, two other forms are also recognized: that due to a disorder of T lymphocyte regulation and that due to production of autoantibodies against T and B lymphocytes. Called also *common variable agammaglobulinemia* or *hypogammaglobulinemia.*

i. with elevated IgM, i. with hyper-IgM, a rare syndrome characterized by elevated immunoglobulin M levels and decreased levels of G and A immunoglobulins, associated with recurrent pyogenic infections, and possibly caused by failure of IgM-producing cells to switch to production of IgC and IgA. Most cases appear to exhibit X-linked recessive inheritance. Called also *i. with elevated* (or *increased*) *IgM.*

severe combined i. (SCID), a group of rare congenital disorders characterized by gross impairment of both humoral and cell-mediated immunity and absence of T lymphocytes; some forms are also characterized by a lack of B lymphocytes. In most cases all classes of immunoglobulins are nearly or completely absent, and there is marked lymphocytopenia. Persistent diarrhea, chronic mucocutaneous candidiasis, and failure to thrive occur in infancy. Blood transfusions can result in graft-versus-host disease and routine vaccinations in fatal infection. Unless immune function is restored by a histocompatible bone marrow or fetal tissue transplant or the patient is kept in gnotobiotic isolation, death from opportunistic infection usually occurs before the first birthday. In approximately 50 per cent of cases, the disorder is X-linked and due to a defect in the γ chain of the receptor for IL-2 and other interleukins. B lymphocyte numbers are usually normal. The remaining 50 per cent of cases are of autosomal recessive inheritance and have varying etiologies, with approximately half of these due to a defect in either adenosine deaminase or, rarely, purine-nucleoside phosphorylase activity. A rare type of the autosomal recessive form is called *reticular dysgenesis.*

i. with short-limbed dwarfism, short-limbed dwarfism marked by short, pudgy hands, redundant skin, and hyperextensible joints of the hands and feet associated with immunodeficiency, which may be either antibody or cellular or combined.

i. with thymoma, an immunodeficiency disorder in which thymoma, usually of the benign spindle-cell type, is associated with hypogammaglobulinemia; deficiencies of cell-mediated immunity, such as eosinopenia, hypoplastic or aplastic anemia, or autoimmune diseases, may occur also. Removal of the thymoma does not cure the immunodeficiency, and patients suffer from recurrent severe infections.

im·mu·no·de·fi·cient (im″u-no-də-fish′ənt) immunocompromised.

im·mu·no·de·pres·sion (im″u-no-də-presh′ən) immunosuppression.

im·mu·no·de·pres·sive (im″u-no-də-pres′iv) immunosuppressive.

im·mu·no·der·ma·tol·o·gy (im″u-no-dər″mə-tol′ə-je) the study of immunologic phenomena as they affect skin disorders and their treatment or prophylaxis.

im·mu·no·de·tec·tion (im″u-no-de-tek′shən) detection of a substance or reaction by means of the specific interaction of antibody with antigen.

im·mu·no·de·vi·a·tion (im″u-no-de″ve-a′shən) split tolerance, def. 2.

im·mu·no·di·ag·no·sis (im″u-no-di″əg-no′sis) diagnosis based on blood serum reactions to antigens; serodiagnosis.

im·mu·no·dif·fu·sion (im″u-no-di-fu′zhən) [MeSH: Immunodiffusion] any technique involving diffusion of antigen or antibody through a semisolid medium, usually agar or agarose gel, resulting in a precipitin reaction. Precipitin lines or bands form where the concentrations of antigen and antibody are serologically equivalent.

radial i. (RID), single radial diffusion.

im·mu·no·dom·i·nance (im″u-no-dom′i-nəns) the degree to which a subunit of an antigenic determinant is involved in binding or reacting with specific antibody.

im·mu·no·dom·i·nant (im″u-no-dom′i-nənt) denoting the subunits of the antigenic determinant group that most influence the specificity of the induced antibodies.

im·mu·no·elec·tro·pho·re·sis (im″u-no-e-lek-tro-fo-re′sis) [MeSH: Immunoelectrophoresis] a technique combining protein electrophoresis and double immunodiffusion; proteins are separated by agarose gel electrophoresis; then specific antisera are placed in a trough cut parallel to the protein track, and the proteins and antibodies are allowed to diffuse through the gel, the proteins diffusing radially from their electrophoretic placement and the antibodies diffusing perpendicularly from the trough, resulting in a distinct elliptical precipitin arc for each protein detectable by the antiserum. Abbreviated IEP.

counter i., counterimmunoelectrophoresis.

countercurrent i., counterimmunoelectrophoresis.

crossed i., a combination of protein electrophoresis and rocket immunoelectrophoresis; protein antigens are separated by agarose gel electrophoresis; then a strip containing the separated antigens is cut out and placed in a trough in a gel containing antiserum, and an electric field perpendicular to the trough is applied, producing a "rocket" precipitin pattern for each antigen.

rocket i., one-dimensional single electroimmunodiffusion; a technique in which antigen is placed in a row of wells in an agar plate containing antiserum and an electric field perpendicular to the line of wells is applied; this drives the antigen through the gel, forming a spike or "rocket" precipitin pattern trailing away from each well. The length of the rocket is proportional to the amount of antigen placed in the well. Called also *Laurell technique.*

im·mu·no·fer·ri·tin (im″u-no-fer′i-tin) an antibody labeled with ferritin; when combined with antigen, the antigenic determinant sites are visible under the electron microscope.

im·mu·no·fil·tra·tion (im″u-no-fil-tra′shən) the purification of antigen or antibody using an immunoadsorbent.

im·mu·no·flu·o·res·cence (im″u-no-floo″o-res′əns) any immunohistochemical method using antibody labeled with a fluorescent dye; called *direct* if a specific antibody or antiserum is conjugated with a fluorochrome and used as a specific fluorescent stain and *indirect* if the fluorochrome is attached to an antiglobulin, and if tissue constituent is stained using an unlabeled specific antibody and the labeled antiglobulin, which binds the unlabeled antibody.

im·mu·no·gen (im′u-no-jən) a substance capable of inducing an immune response, in most contexts synonymous with antigen; in some contexts immunogen is used to draw a distinction with substances capable of reacting only with antibody (antigens or haptens) or to denote a form of an antigen that induces an immune response as opposed to a tolerogen, a form that induces tolerance.

im·mu·no·ge·net·ic (im″u-no-jə-net′ik) pertaining to immunogenetics.

im·mu·no·ge·net·ics (im″u-no-jə-net′iks) [*immuno-* + *genetics*] [MeSH: Immunogenetics] the study of the genetics of the immune response, e.g., the study of immune response genes; or the association of HLA antigens with disease susceptibility; or the generation of antibody diversity.

im·mu·no·gen·ic (im″u-no-jen′ik) producing immunity; evoking an immune response.

im·mu·no·ge·nic·i·ty (im″u-no-jə-nis′i-te) the property that endows a substance with the capacity to provoke an immune response, or the degree to which a substance possesses this property.

im·mu·no·glob·u·lin (im″u-no-glob′u-lin) any of the structurally related glycoproteins that function as antibodies, divided into five classes (IgM, IgG, IgA, IgD, and IgE) on the basis of structure and biologic activity. The basic structural unit of the immunoglobulin molecule, referred to as a monomer, is a Y-shaped molecule composed of two heavy (H) chains and two light (L) chains (see accompanying illustration). IgD, IgG, and IgE occur only as monomers; IgA and IgA may occur as monomers or polymers. The polymeric forms contain an additional polypeptide called the J chain, and secretory IgA contains another structure called the secretory component (SC). Each chain consists of a variable region (V_H or V_L) and a constant region (C_H or C_L), which are coded for by different genes; two of the V_H and V_L regions make up the antigen-binding site, two of each "arm" (Fab region) of the monomer. An individual can make about 10^4 different V_H regions and 10^3 V_L regions, which combine to make about 10^7 different antigen-binding sites, each with a distinct antigenic specificity. Parts of the C_H regions make up the Fc (crystallizable region) of the monomer, which contains various sites responsible for the biological activity of the molecule. In any one immunoglobulin molecule, all of the H chains are identical, as are the L chains. The C_H region determines both the heavy chain class to which the H chain belongs and the immunoglobulin class to which the whole molecule belongs. The H chain classes are denoted by the Greek letters (μ, δ, γ, ϵ, and α) corresponding to the Latin letters of the immunoglobulin classes, e.g., μ to IgM. There are two types of light chain (denoted κ and λ), either of which may combine with any of the heavy chains and thus occur in any of the immunoglobulin classes. In human immunoglobulins, three of the classes (IgG, IgA, IgD) have subclasses; i.e., there are several similar but distinct